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Proposed Re-evaluation Decision PRVD2017-04

Diflufenzopyr-sodium

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Publications
Pest Management Regulatory Agency
Health Canada
2720 Riverside Drive
A.L. 6607 D
Ottawa, Ontario K1A 0K9

Internet: pmra.publications@hc-sc.gc.ca
healthcanada.gc.ca/pmra
Facsimile: 613-736-3758
Information Service:
1-800-267-6315 or 613-736-3799
pmra.infoserv@hc-sc.gc.ca

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Overview

Proposed Re-evaluation Decision for Diflufenzopyr-Sodium

After a re-evaluation of the herbicide diflufenzopyr-sodium, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration of products containing diflufenzopyr-sodium for sale and use in Canada.

An evaluation of available scientific information found that products containing diflufenzopyr-sodium do not present unacceptable risks to human health or the environment when used according to the revised label directions. As a requirement of the continued registration of diflufenzopyr-sodium uses, new risk reduction measures are proposed to be included on the labels of all products.

This proposal affects all end-use products containing diflufenzopyr-sodium registered in Canada.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for diflufenzopyr-sodium and presents the reasons for the proposed re-evaluation decision.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides additional technical information on the assessment of diflufenzopyr-sodium.

The PMRA will accept written comments on this proposal up to 90 days from the date of publication of this document. Please forward all comments to Publications (see contact information on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment.

What is Diflufenzopyr-sodium?

Diflufenzopyr-sodium is a post-emergent herbicide which is applied using ground application equipment to field corn, non-cropland, fallow cropland, pasture and rangeland for the control of broadleaf weeds. Diflufenzopyr-sodium inhibits the transport of naturally occurring auxin and synthetic auxin-like compounds in plants.

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1 *"Consultation statement" as required by subsection 28(2) of the Pest Control Products Act.*

Health Considerations

Can Approved Uses of Diflufenzopyr-Sodium Affect Human Health?

Diflufenzopyr-sodium is unlikely to affect your health when used according to the revised label directions.

People could be exposed to diflufenzopyr-sodium by working as a mixer/loader/applicator, by entering treated sites, or by consuming food and water. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). As such, sex and gender are taken into account in the risk assessment. Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Occupational exposures to workers mixing, loading and applying the herbicide using a ground sprayer or handheld sprayer, as well as to workers re-entering treated sites, are not of concern when diflufenzopyr-sodium is used according to the label directions, which include protective measures. Taking into consideration the current use of diflufenzopyr-sodium in Canada, the risk to workers is not a concern.

Residential exposure to diflufenzopyr is not expected based on the use pattern. Dietary exposure to diflufenzopyr-sodium through consumption of food commodities and drinking water is not of concern. Additional label statements are proposed to be added to the product labels to update to the current labelling standard.

Maximum Residue Limits

The *Food and Drug Act* prohibits the sale of adulterated food; that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in or on certain foods. Food containing a pesticide residue that is at or below the established MRL does not pose an unacceptable health risk. Canadian MRLs are currently specified for some commodities, as found in the MRL database on the Pesticides and Pest Management portion of the Health Canada website. Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specific MRL, are regulated under subsection B.15.002(1) of the Food and Drug Regulations, which requires that residues not exceed 0.1 ppm.

No changes are proposed to the current MRLs for diflufenzopyr-sodium.

Environmental Considerations

What Happens When Diflufenzopyr-Sodium is Introduced into the Environment?

Diflufenzopyr-sodium is not expected to pose unacceptable risk to the environment when used according to the proposed label directions.

Diflufenzopyr-sodium can enter the environmental when it is applied as an herbicide to fields. In soil, diflufenzopyr-sodium breaks down quickly and is not expected to persist. In water, diflufenzopyr-sodium mixes readily and breaks down more slowly than in soil. Diflufenzopyr is not expected to enter the air or be transported over long distances. Diflufenzopyr-sodium has properties that indicate that it has a moderate to high potential to be mobile in soils, but because it breaks down quickly in soil, it is unlikely to reach groundwater. Diflufenzopyr is not expected to build-up in the tissues of organisms.

Diflufenzopyr is toxic to non-target plants and aquatic organisms. Updated spray buffer zones are proposed to reduce exposure to non-target plants and aquatic organisms. Updated environmental label statements are required. There are no concerns about diflufenzopyr-sodium or its major breakdown products affecting any other non-target organisms. Diflufenzopyr-sodium is not expected to pose a risk of concern to non-target terrestrial and aquatic species when used according to the proposed label directions.

Value Considerations

What is the Value of Diflufenzopyr-sodium

Diflufenzopyr-sodium is a commonly used post-emergence herbicide in field corn (especially conventional glyphosate intolerant varieties), which is one of the most important arable crops grown in Eastern Canada. In Western Canada, it is a significant component of chemfallow practices and provides an additional weed management option for post-harvest weed control.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human health and the environment. These directions must be followed by law. As a result of the re-evaluation of diflufenzopyr-sodium, PMRA is proposing further risk-reduction measures related to the environment for product labels:

- Buffer zone and label statements to protect non-target terrestrial plants and aquatic organisms.

In addition, the following measures are required to update to the current labelling standard:

- Restricted-entry interval of 12 hours.
- Precautionary label statement to minimize bystander exposure from spray drift.
- Environmental hazard label statements.

What Additional Scientific Information is Required?

No additional data are required.

Next Steps

Before making a final re-evaluation decision on diflufenzopyr-sodium, PMRA will consider any comments received from the public in response to this consultation document. A science-based approach will be applied in making a final decision on diflufenzopyr-sodium. PMRA will then publish a Re-evaluation Decision[2] that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA response to these comments.

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2 *"Decision statement" as required by subsection 28(5) of the Pest Control Products Act.*

Science Evaluation

1.0 Introduction

Following the re-evaluation announcement for diflufenzopyr-sodium, the registrant of the technical grade active ingredient in Canada indicated that they intended to provide continued support for all uses included on the labels of the commercial class end-use products in Canada. Currently registered products containing diflufenzopyr-sodium are listed in Appendix I.

2.0 Use Description of Diflufenzopyr-sodium

Diflufenzopyr-sodium is a post-emergent herbicide used for the control of broadleaf weeds. It is applied using ground application equipment to field corn, non-cropland, fallow cropland, pasture and rangeland. Diflufenzopyr-sodium can be applied once per year using a groundboom or handheld sprayer at a maximum application rate of 57 g a.e./ha.

3.0 The Technical Grade Active Ingredient, Its Properties and Uses

3.1 Identity of the Technical Grade Active Ingredient

Common name		Sodium diflufenzopyr
Function		Herbicide
Chemical Family		Semicarbazone
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	Sodium 2-{(*E*)-1-[4-(3,5-difluorophenyl)semicarbazono]ethyl} nicotinate
2	**Chemical Abstracts Service (CAS)**	sodium 2-[(1*E*)-1-[2-[[(3,5-difluorophenyl)amino]carbonyl]hydrazinylidene]ethyl]-3-pyridinecarboxylate
CAS Registry Number		109293-98-3
Registration Number		29004

3.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	$<1.33 \times 10^{-5}$ Pa for the free acid. Not required for the salt.
Ultraviolet (UV) / visible spectrum	λ (nm) ε (L/mol-cm) pH 204 1.8×10^4 1.94 232 1.15×10^4 1.94 266 7.02×10^3 1.94 316 5.96×10^3 1.94 204 2.86×10^4 7.06 236 2.27×10^4 7.06 296 1.63×10^4 7.06 236 2.35×10^4 10.08 296 1.68×10^4 10.08 No absorbance observed >350 nm.
Solubility in water at 25°C	42.5 g/L
n-Octanol/water partition coefficient	pH K_{ow} 5.0 2.76 7.0 0.34 9.0 0.17
Dissociation constant	pKa = 3.18

4.0 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much greater) than levels to which humans are normally exposed when pesticide products are used according to label directions. Based on the registered use pattern, exposure to diflufenzopyr-sodium may occur through consuming food and drinking water, working as a mixer/loader/applicator, or by entering treated sites.

When assessing health risks, the PMRA considers two key factors – the dose levels at which no adverse health effects occur (that is, the No Observed Adverse Effect Level [NOAEL]), and the dose levels to which people may be exposed. The NOAELs used to assess risks are established to protect the most sensitive human population, for example, children and nursing mothers.

As such, sex and gender are taken into account in the risk assessment. Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

4.1 Toxicological Summary

The database for diflufenzopyr-sodium is considered complete and no data deficiencies have been identified by the PMRA.

Diflufenzopyr-sodium is partially absorbed and not extensively metabolized. It is rapidly eliminated, primarily via the feces. It has a low acute toxicity via oral, inhalation and dermal routes of exposure. It was not irritating to skin but was minimally irritating to the eyes. It is not a skin sensitizer.

No evidence of toxicity was observed in rabbits following a 21-day dermal exposure up to 1000 mg/kg bw/day.

In short term dietary toxicity studies in mice, there were no treatment related effects; however, a decrease in body weight gain, increase in alanine amino transferase, increased cholesterol and an increased incidence of foamy macrophages in the lungs were noted in rats. In the 90-day dog study, treatment related erythroid hyperplasia in the bone marrow, extramedullary hematopoiesis in the liver and hemosiderin deposits in the Kupffer cells was noted.

In the one year dog study, treatment related effects included decreases in body weight gain and increased erythroid hyperplasia in the femoral and sternal bone marrow of both sexes. Food efficiency was decreased in females only. There were hemosiderin deposits in the kidney, liver and spleen, reddish discoloration of the diaphysis of the femur and mild to moderate reticulocytosis in both sexes.

In the long-term dietary study, no treatment related effects were noted up to the limit dose in mice. In the rat there were decreases in body weight and body weight gain seen primarily in the second year of a long term study. There was no evidence of carcinogenicity in either species, and no evidence of genotoxic potential of diflufenzopyr-sodium was observed.

In the rat developmental toxicity study there was no evidence of maternal or developmental toxicity at any dose, however, in the rabbit developmental toxicity study, effects included abortions and maternal death, which occurred at the same dose late in gestation. In the reproductive toxicity study, effects consisted of an increase in total post implantation loss, and a decrease in live-birth index at doses that also caused parental toxicity.

There was no evidence of neurotoxicity in either the acute or short term neurotoxicity studies.

Appendix II summarizes the diflufenzopyr-sodium toxicology endpoints used in human health risk assessments by the PMRA.

4.2 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes and/or schools, the *Pest Control Products Act* requires the application of additional 10-fold factor to threshold effects to take into account the completeness of the data with respect to the exposure of, and toxicity to, infants and children, and potential prenatal and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the toxicity to infants and children, the database for diflufenzopyr-sodium contains the standard complement of required studies including developmental toxicity studies in rats and rabbits and a reproductive toxicity study in rats.

With respect to potential prenatal and postnatal toxicity, no evidence of sensitivity of the young compared to parental animals was observed in the rat developmental and reproductive toxicity studies. In the two generation rat toxicity study, parental females experienced increased post implantation loss and a corresponding decrease in live birth index, in addition to decreased body weight and body weight gain. Offspring effects included decreased live birth and viability indices, decreased body weight and body weight gains pre-weaning, and an increased proportion of runts as well as offspring with no milk in the stomach. In the rabbit developmental toxicity study, effects included abortions and maternal death which occurred at the same dose, late in gestation.

Overall, effects on the young are well characterized and there is a low level of concern for sensitivity of the young. The abortions in rabbits and the post implantation loss in rats were considered serious endpoints although the concern for these findings was tempered by the presence of maternal toxicity. Therefore, the *Pest Control Products Act factor* (PCPA factor) was retained at 3-fold when using the rabbit developmental toxicity study to establish the point of departure for scenarios assessing risk to women of child bearing age. For all other scenarios, the endpoint selected was considered protective of prenatal and postnatal concerns; therefore, the PCPA factor was reduced to 1-fold.

4.3 Occupational Exposure

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a Margin of Exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

Workers can be exposed to diflufenzopyr-sodium through mixing, loading or applying the product using a field sprayer (ground boom or hand held sprayer) or when entering a treated site to conduct activities such as scouting and/or handling treated crops.

4.3.1 Mixer/Loader/Applicator Exposure and Risk

Mixer/loader/applicator exposure is expected to be mainly via dermal and inhalation routes. Based on the diflufenzopyr-sodium use pattern, the following scenarios were assessed:

- Short- and intermediate-term exposure from open mixing/loading of the wettable granule formulation and application using an open cab groundboom sprayer.
- Short- and intermediate-term exposure from open mixing/loading of the wettable granule formulation and application using a hand-held sprayer.

Exposure for workers mixing/loading a wettable granule and applying the pesticide using an open cab groundboom or handheld sprayer was estimated using the most conservative scenario per application method and unit exposure values from the Pesticide Handlers Exposure Database (PHED), version 1.1. The assessment assumed that workers were wearing the current label personal protective equipment (PPE) consisting of a single layer of clothing plus gloves. The assessments were based on maximum application rates and assuming an area treated per day up to 360 ha for groundboom and 150 L handled per day for handheld equipment.

The combined short- to intermediate-term dermal and inhalation MOEs (>1200) for the wettable granule formulation were above the target MOE (300). On this basis, the risks for workers mixing, loading and applying the product are not of concern.

Requirements for personal protective equipment included on the product labels (which include a single layer of clothing and chemical-resistant gloves) are adequate and no additional mitigation measures are proposed.

4.3.2 Post-application Exposure and Risk

For workers entering treated fields to conduct post-application activities, dermal exposure is considered to be the primary route of exposure. Diflufenzopyr-sodium is relatively non-volatile (vapour pressure of $<1 \times 10^{-7}$ mm Hg at 25°C) and meets the North American Free Trade Agreement (NAFTA) criterion for an inhalation waiver based on low volatility due to a vapour pressure of less than 7.5×10^{-4} mm Hg (NAFTA, 1999). Thus, inhalation exposure is considered minimal and is not expected to be of concern for post-application activities.

Dermal exposure estimates for post-application workers were calculated by coupling dislodgeable foliar residue values with activity-specific transfer coefficients and the dermal absorption factor for diflufenzopyr-sodium. The dermal MOEs (>5100) were above the target MOE (300) on the day of application. On this basis, post-application risk for workers entering treated fields is not of concern. Not all labels currently include a restricted-entry interval. Therefore, it is proposed to update labels to indicate a minimum restricted-entry interval of 12 hours (Appendix III).

4.4 Non-occupational Exposure

4.4.1 Residential Exposure and Risk

There are no residential uses of diflufenzopyr-sodium nor is it expected that the commercial products would be applied in residential areas. A standard statement is proposed to specify that application is limited to non-residential areas and should be applied when the spray is unlikely to drift into areas of human habitation or activity such as houses, cottages, schools and recreational areas. The proposed label statement is listed in Appendix III.

4.4.2 Dietary Exposure and Risk

In a dietary exposure assessment, the PMRA determines how much of a pesticide residue, including residues in milk, milk products, eggs, and meat, may be ingested with the daily diet (food and drinking water).

These dietary assessments are age-specific and incorporate the different eating habits of the population at various stages of life (infants, children, adolescents, adults and seniors). For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults.

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore an acute dietary risk assessment was not conducted.

The chronic dietary exposure was calculated by using the average consumption of different foods and the estimated residue values of diflufenzopyr-sodium on those foods using Canadian MRL level residues and US tolerances for all food commodities with default food processing factors and the assumption that 100% of the crop was treated. For water, the estimated concentrations in potential drinking water sources (groundwater and surface water) were generated using modeling and conservative assumptions with respect to environmental fate, application rate and timing, geographic scenario, and weather data. The expected intake of residues was then compared to the acceptable daily intake (ADI), which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. When the calculated intake of residues from all food sources (including water) is less than the ADI, then chronic dietary exposure is not of concern.

The ADI for diflufenzopyr-sodium was determined to be 0.26 mg/kg bw/day based upon a NOAEL of 26 mg/kg bw/day and a CAF of 100 (see Appendix II). The basic chronic dietary exposure to diflufenzopyr-sodium from food plus drinking water was less than 1% of the ADI. The highest exposed subpopulation was children 1-2 years old. On this basis, dietary exposure to diflufenzopyr-sodium residues is not of concern.

4.5 Aggregate Exposure and Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water, residential and other non-occupational sources as well as from all known or plausible exposure routes (oral, dermal and inhalation).

As residential exposure is not expected, aggregate exposure is limited to food and drinking water only which is not of concern (see section 4.5).

4.6 Cumulative Exposure and Risk

The *Pest Control Products Act* requires that the PMRA consider the cumulative exposure to pesticides with a common mechanism of toxicity. For the current re-evaluation, the PMRA did not identify information indicating that diflufenzopyr shares a common mechanism of toxicity with other pest control products. Therefore there is no requirement for a cumulative assessment at this time.

5.0 Environment

Diflufenzopyr-sodium may enter the environment through application to fields and non-crop areas. There is a potential that non-target terrestrial and aquatic habitats may be exposed to the chemical as a result of spray drift or runoff.

5.1 Environmental Fate

The physical and chemical properties of diflufenzopyr-sodium are summarized in section 3.1. The environmental fate properties of diflufenzopyr-sodium are summarized in Appendix IV.

In soil, diflufenzopyr-sodium is non-persistent and breaks down readily through aerobic soil biotransformation. The major transformation product,M9, is produced in aerobic soil biotransformation studies. In water, diflufenzopyr-sodium is slightly persistent and its major transformation products, in water, included M1 and M9 which are not expected to persist in aerobic aquatic environments. Diflufenzopyr-sodium has a moderate to very high potential for mobility.

5.2 Environmental Exposure and Risk Assessment

A summary of effects of diflufenzopyr-sodium on terrestrial and aquatic organisms is presented in Appendix V.

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil, and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties, and environmental fate properties, including the dissipation of the pesticide between applications.

Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants.

Initially, a conservative screening-level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate with an appropriate toxicity value (RQ = exposure/toxicity/uncertainty factor). The RQ is then compared to the level of concern (LOC < 1, and 0.4 for acute bee endpoints), and if the RQ is below the LOC, the risk is considered negligible and no further risk characterization is necessary. If the value is equal to or greater than the LOC (≥1), then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints.

For the screening-level assessment, diflufenzopyr-sodium, EECs were based on the maximum label application rate (57 g a.i//ha). The toxicity endpoints evaluated were chosen from the most sensitive species to act as surrogates for the wide range of species that can be potentially exposed following treatment with diflufenzopyr-sodium. A summary of effects of diflufenzopyr-sodium on terrestrial and aquatic organisms can be found in Appendix V.

5.2.1 Terrestrial Organisms

The screening-level risk assessment indicates that diflufenzopyr-sodium poses negligible risk to earthworms, honeybees, birds and mammals. In addition, conservative estimates of exposure indicate that it is unlikely that a chronic risk will be posed to bee larva or adults through this use pattern.

The screening-level assessment indicated diflufenzopyr-sodium may pose a risk to non-target plants when applied at the maximum application rate (RQ = 19.4). A refined assessment was performed for spray drift and it was determined that spray buffer zones of one meter provide adequate protection for non-target terrestrial plants. Proposed buffer zones are identified in Appendix III.

5.2.2 Aquatic Organisms

Diflufenzopyr-sodium poses negligible risk to daphnids, fish, oyster and shrimp. The screening-level assessment indicated that diflufenzopyr-sodium could pose a risk to algae (RQs = 1.4 and 2.4), diatoms (RQ= 6.3) and aquatic plants (RQ = 4.9). A refined risk assessment for spray drift indicated that there are no risks of concern for aquatic organisms and aquatic buffer zone are not required. Diflufenzopyr-sodium labels include standard wording regarding run-off mitigation for the protection of aquatic organisms .

6.0 Value

Diflufenzopyr-sodium provides control of not only annual broadleaved weeds, but also hard-to-control perennial weeds including dandelion, narrow leaf hawk's beard, Canada thistle and kochia.

Diflufenzopyr-sodium has value as a herbicide for both Eastern and Western Canadian growers. It is a commonly-used post-emergence herbicide in field corn (especially conventional non-glyphosate tolerant varieties). Field corn is one of the most important arable crops grown in Eastern Canada. Diflufenzopyr-sodium is a significant component of chemfallow practices in Western Canada. Diflufenzopyr-sodium provides an additional weed management option for post-harvest, where alternatives are limited. The use of diflufenzopyr-sodium in chemfallow and post-harvest is helpful to manage herbicide resistance to others common modes of action.

7.0 Pest Control Product Policy Considerations

7.1 Toxic Substances Management Policy Considerations

Diflufenzopyr-sodium was assessed in accordance with PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, and does not meet the Track 1 criteria.

7.2 Contaminants of Health or Environmental Concern

During the re-evaluation of diflufenzopyr-sodium, contaminants in the technical were compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[3]. The list is used as described in the PMRA Notice of Intent NOI2005-01 and is based on existing policies and regulations including: DIR99-03; and DIR2006-02, and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol).

Based on the manufacturing process used, impurities of human health or environmental concern as identified in the Canada Gazette are not expected to be present in the product.

8.0 Incident Reports

As of 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. As of 25 January 2017, the PMRA had not received any incident reports associated with diflufenzopyr-sodium.

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[3] *Canada Gazette, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641 - 2643: List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern and in the order amending this list in the Canada Gazette, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613, Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

9.0 Organisation for Economic Co-operation and Development

Canada is part of the Organisation for Economic Co-operation and Development (OECD), which groups member countries and provides a forum in which governments can work together to share experiences and seek solutions to common problems.

As part of the re-evaluation of an active ingredient, the PMRA takes into consideration recent developments and new information on the status of an active ingredient in other jurisdictions, including OECD member countries. In particular, decisions by an OECD member country to prohibit all uses of an active ingredient for health or environmental reasons are considered for relevance to the Canadian situation.

Diflufenzopyr-sodium is currently acceptable for use in the United States. As of January 30, 2017, no decisions by OECD member country to prohibit all uses of diflufenzopyr-sodium for health or environmental reasons have been identified.

10.0 Proposed Re-evaluation Decision

PMRA has determined that products containing diflufenzopyr-sodium for sale and use in Canada are acceptable for continued registration with the revised conditions of use (Appendix III).

List of Abbreviations

ADI	acceptable daily intake
a.e.	acid equivalent
ARfD	acute reference dose
bw	body weight
CAF	Composite Assessment Factor
DT_{50}	dissipation time 50%
EEC	expected environmental concentration
g	gram(s)
ha	hectare
kg	kilogram(s)
K_{oc}	soil organic carbon-water partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
mg	milligram(s)
MOE	margin of exposure
MRL	Maximum Residue Limit
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
OECD	Organization for Economic Co-operation and Development
PCPA	*Pest Control Products Act*
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
pKa	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
REI	restricted-entry interval
SF	Safety Factor
TSMP	Toxic Substances Management Policy
µg	microgram(s)
UF	Uncertainty Factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
λ	wavelength

Appendix I Registered Diflufenzopyr-Sodium Products as of 23 January 2017

Registration Number	Marketing Type	Registrant Name	Product Name	Formulation type	Guarantee
29004	Technical Grade Active Ingredient	BASF Canada Inc.	Sodium Diflufenzopyr Technical Herbicide	Dust	Diflufenzopyr sodium 86.3%
26143	Manufacturing Concentrate		Distinct Herbicide Manufacturing Concentrate	Wettable Granule	Diflufenzopyr sodium 20% Dicamba 50%
25881	Commercial		Distinct Herbicide		
30065			Overdrive Herbicide		

Appendix II Toxicology Endpoints for Use in Health Risk Assessment for Diflufenzopyr-Sodium

Exposure Scenario	Study	Point of Departure and Endpoint	CAF[1] or Target MOE
Acute dietary	Not established. No appropriate endpoint was identified		
Chronic dietary	1-year dog	NOAEL = 26 mg/kg bw/day Based on mild compensatory anaemia and decreased food efficiency	100
	ADI = 0.26 mg/kg bw/day		
Short-term dermal[2] and inhalation[3]	Rabbit developmental	NOAEL of 100 mg/kg bw/day Based on increased abortions and mortality	300 (3× PCPA factor)
Intermediate-term dermal[2] and inhalation[3]			

1 CAF (composite assessment factor) refers to a total of uncertainty and PCPA factors for dietary assessment. MOE refers to a target MOE for occupational and residential assessments. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied.

2 Since an oral NOAEL was selected, a dermal absorption factor of 100% (default value) was used in a route to route extrapolation.

3 Since an oral NOAEL was selected an inhalation absorption factor of 100% (default value) was used in route to route extrapolation.

Appendix III Label Amendments for Commercial Class End-Use Products Containing Diflufenzopyr

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Information on labels of currently registered products should not be removed unless it contradicts the label statements provided below.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

I) Under **PRECAUTIONS**, the following statements must be added:

"Do not enter or allow workers entry into treated areas during the restricted-entry interval (REI) of 12 hours."

"DO not use in residential areas. Residential areas are defined as any use site where bystanders, including children, could be exposed during or after application. This includes homes, schools, parks, playgrounds, playing fields, public buildings, or any other area where the general public, including children, could be exposed."

"Apply only when the potential for drift to areas of human habitation or areas of human activity such as houses, cottages, schools and recreational areas is minimal. Take into consideration wind speed, wind direction, temperature inversions, application equipment and sprayer settings."

II) The following statements must be included in a section entitled **ENVIRONMENTAL HAZARDS**.

"TOXIC to non-target terrestrial plants. Observe buffer zones specified under DIRECTIONS FOR USE."

"To reduce runoff from treated areas into aquatic habitats, avoid application to areas with a moderate to steep slope, compacted soil, or clay."

"Avoid application when heavy rain is forecast."

"Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body."

III) The following statements must be included in a section entitled **DIRECTIONS FOR USE**.

"Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. Boom height must be 60 cm or less above the crop or ground."

"DO NOT apply by air."

"As this product is not registered for the control of pests in aquatic systems, DO NOT use to control aquatic pests."

"DO NOT contaminate irrigation or drinking water supplies or aquatic habitats by cleaning of equipment or disposal of wastes."

Buffer Zones:

Use of the following spray methods or equipment **DO NOT** require a buffer zone: hand-held or backpack sprayer and spot treatment.

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, riparian areas and shrublands).

Method of application	Crop	Buffer Zones (metres) Required for the Protection of Terrestrial habitat:
Field Sprayer	Field corn, non-cropland, pasture, rangeland	1

For tank mixes, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture and apply using the coarsest spray (ASAE) category indicated on the labels for those tank mix partners."

Appendix IV Environmental Fate of Diflufenzopyr-sodium

Fate process	Endpoint	Interpretation*
AQUATIC		
Hydrolysis	$T_{1/2}$: 12.9 d at pH 5 $T_{1/2}$: 23.9 d at pH 7 $T_{1/2}$: 25.6 d at pH 9	An important route of transformation in the environment.
Phototransformation in water	$T_{1/2}$: 6.8 d at pH 5 $T_{1/2}$: 16.8 d at pH 7 $T_{1/2}$: 13.4 d at pH 9	An important route of transformation under acidic environmental conditions.
Aerobic sediment/ water	$T_{1/2}$: 26 d, phenyl label $T_{1/2}$: 25 d, pyridyl label	Slightly persistent in aerobic water-sediment systems.
Anaerobic sediment/ water	$T_{1/2}$: 20 d, phenyl label $T_{1/2}$: 26 d, pyridyl label	Slightly persistent in anaerobic water sediment systems.
TERRESTRIAL		
Hydrolysis	$T_{1/2}$: 12.9 d at pH 5 $T_{1/2}$: 23.9 d at pH 7 $T_{1/2}$: 25.6 d at pH 9	An important route of transformation.
Phototransformation on soil	$T_{1/2}$: 14 d	Not an important route of transformation.
Aerobic soil biotransformation	$T_{1/2}$: 8 d $T_{1/2}$: 10 d	Non persistent.
Adsorption/ desorption	Adsorption K_{oc} (diflufenzopyr): 18–156 mL/g Adsorption K_{oc} (M1): 140–596 mL/g Adsorption K_{oc} (M9): 385–3668 mL/g	Moderate to very high mobility. Low to high mobility. Slight to moderate mobility.
Field dissipation of Distinct® herbicide on bare plots	**Ontario, Canada** DT_{50}: 4 d DT_{90}: 8.45 d	Non-persistent. Did not leach below the top 15 cm of soil.

* Classification of persistence in soil according to Goring et al. (1975); classification of persistence in water according to McEwan and Stephenson (1979); classification of adsorption/ desorption and mobility according to McCall et al. (1981).

Appendix V Summary of Effects of Diflufenzopyr-sodium on Terrestrial and Aquatic Organisms

Organism	Exposure	Endpoint value	Degree of Toxicity[a]
Earthworm (*Eisenia foetida*)	14-day chronic	LC50: >1000 mg a.i./kg soil NOEC (mortality): 500 mg a.i./kg soil	Non-lethal > 500 mg a.i./kg substrate
Bee[1]	48-hour chronic acute contact	LC50: > 25 µg a.i./bee NOEC (mortality): 25 µg a.i./bee EEC[2]: 0.137 µg a.i./bee RQ: <0.005	Non-toxic (Atkins et al. 1981)
	48-hour acute oral	LC50: > 25 µg a.i./bee NOEC (mortality): 25 µg a.i./bee EEC[2]: 1.65 µg a.i./bee RQ: <0.066	Non-toxic (Atkins et al. 1981)
Bobwhite quail (*Colinus virginianus*)	14-day chronic oral	LD50: >1868 mg a.i./kg bw NOEL (mortality): 1868 mg a.i./kg bw	At most slightly toxic
	5-day dietary	LC50: >4608 mg a.i./kg diet NOEC (food consumption + body weight): 4608 mg a.i./kg diet	Practically non-toxic
Mallard duck (*Anas platyrhynchos*)	5-day dietary	LC50: >4608 mg a.i./kg diet NOEC ((food consumption + body weight): 2591 mg a.i./kg diet	At most slightly toxic
	22-week reproduction	NOEC (reproductive parameters, hatchling + parental): 1000 mg a.i./kg diet NOEC (reproductive parameters, hatchling + parental): 1000 mg a.i./kg diet	--
Mammals			
Rats	Chronic oral	LD50: >5000 mg/kg bw	Low toxicity
	13-week dietary	NOAEL: 5000 mg/kg diet	---
	Reproduction	NOAEL reproduction: 8000 mg/kg diet	---
Mouse	13-week dietary	NOAEL: 7000 mg/kg diet	---
Vascular plants			
Vascular plants	Phytotoxicity (radish)	EC25: 14.7 g product/ha NOEC: 35 g product/ha	
	Dry plant weight (tomato)	EC25: 21.4 g product/ha NOEC: 4.4 g product/ha	

	Shoot length (tomato)	EC25: 31.8 g product/ha NOEC: 35 g product/ha

[a] Based on the classification scheme of United States Environmental Protection Agency (1985) unless otherwise stated.
Note: All studies were conducted with the active ingredient, unless otherwise stated (for example, vascular plants).
[1] Based on a back calculation for larval bees and adult bees using a conservative estimate of exposure from corn metabolism studies (to derive amount of active in corn pollen, 0.4 ppm), the endpoint would need to be >8000 times and > 25000 times more sensitive than the adult oral endpoint, for adults and larval (LC50>25 µg a.i./bee), respectively. This is highly unlikely. No risk is expected to adults and larva from chronic exposure.
[2] EECs (expected environmental concentrations) for diet and contact exposure were calculated according to the new pollinator framework as outlined in Pollinator Protection on the Pesticides and Pest Management portion of Health Canada's website. The EEC for contact exposure is calculated by multiplying the single maximum application rate by 2.4 µg a.i./bee. The EEC for adult oral exposure is calculated by multiplying the single maximum application rate by 29 µg a.i./bee.

Group	Organism	Exposure	Test substance	Endpoint	Degree of Toxicity[a]
Freshwater					
Invertebrates	*Daphnia magna*	48-h	Diflufenzopyr-sodium	NOEC (mortality): 9.7 mg a.i./L LC50: 15 mg a.i./L	Slightly toxic
Fish	Rainbow trout (*Oncorhynchus mykiss*)	96-h	Diflufenzopyr-sodium	NOEC (mortality): 80 mg a.i./L LC50: 106 mg a.i./L	Practically non-toxic
	Bluegill sunfish (*Lepomis machrochirus*)	96-h	Diflufenzopyr-sodium	NOEC (mortality): 16 mg a.i./L LC50: >135 mg a.i./L	Practically non-toxic
Algae	Bluegreen (*Anabaena flos-aquae*)	5-d	Diflufenzopyr-sodium	NOEC (biomass): 0.014 mg a.i./L EC50: 0.15 mg a.i./L	No toxicity classification based on study type
			Distinct EUP	NOEC (biomass): 0.0059 mg EUP/L EC50: >0.26 mg EUP/L	No toxicity classification based on study type
	Bluegreen (*Selenastrum capricortumm*)	5-d	Diflufenzopyr-sodium	NOEC (biomass): 0.0078 mg a.i./L EC50: 0.11 mg a.i./L	No toxicity classification based on study type
Diatom	*Naviculla pelliculosa*	5-d	Diflufenzopyr-sodium	NOEC (biomass): 0.003 mg a.i./L EC50: 0.10 mg a.i./L	No toxicity classification based on study type

Group	Organism	Exposure	Test substance	Endpoint	Degree of Toxicity[a]
Aquatic plants	*Lemna minor*	7-d	Diflufenzopyr-sodium	NOEC (biomass): 0.0039 mg a.i./L EC50: >0.35 mg a.i./L	No toxicity classification based on study type
			distinct EUP	NOEC (biomass): 0.0023 mg EUP/L EC50: 0.11 mg EUP/L	No toxicity classification based on study type
Marine					
Invertebrates	eastern oyster (*Crassostrea virginica*	96-h	Diflufenzopyr-sodium	NOEC (shell growth): 31 mg a.i./L EC50: 61 mg a.i./L	Slightly toxic
	mysid shrimp *Mysidopsis bahia*	96-h	Diflufenzopyr-sodium	NOEC (mortality): 4.4 mg a.i./L LC50: 18.9 mg a.i./L	Slightly toxic
Fish	Sheepshead minnow (*Cyprinodon variegatus*)	96-h	Diflufenzopyr-sodium	NOEC (mortality): 138 mg a.i./L LC50: >138 mg a.i./L	Practically non-toxic
Diatom	*Skeletoneum costatum*	5-d	Diflufenzopyr-sodium	NOEC (mortality): 0.0064 mg a.i./L EC50: 0.12 mg a.i./L	No toxicity classification based on study type

[a] Based on the classification scheme of United States Environmental Protection Agency (1985) unless otherwise stated

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